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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/945,325	08/31/2001	Everett C. Pesci	UIZ-068CP	1369

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LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER

HUANG, EVELYN MEI

ART UNIT	PAPER NUMBER
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1625

DATE MAILED: 09/09/2002

7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/945,325

Applicant(s)

PESCI ET AL.

Examiner

Evelyn Huang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-64 is/are pending in the application.
- 4a) Of the above claim(s) 43-45 and 49-64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-42 and 46-48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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1. Claims 1-64 are pending.

Election/Restrictions

2. In response to the restriction requirement mailed on 5-21-2002, applicant has elected the invention of Group I, claims 13, 19 and claims 1-12, 14-18, 20-40, 46-48 in part, and the method of use of Group III with traverse. Claims of the other groups of invention are withdrawn from further consideration as being drawn to the non-elected inventions.

Applicant argues that all the claims are different embodiments of a single inventive concept and the search would not be a serious burden for the examiner.

On the contrary, a single inventive concept exists only where compounds included within a Markush group share a *common utility and share a substantial structural feature disclosed as being essential to that utility*. The Markush elements in the instant claims are so diverse in scope that a common nucleus essential to that utility is lacking. For example, while the compound of group I wherein Y is N has been shown to be useful for treating gastroduodenal disorders (Dekker, 5942619), compound of group II wherein Y is O is shown to be a melanin biosynthesis inhibitors (JP 07188208).

The structure of the inhibitor of autoinducer activity of 2-heptyl-3-hydroxy-4-quinoline (Group VII), and the structure of the analog compound of 2-heptyl-3-hydroxy-4-quinoline of (Group VIII) have not been recited in the claims or in the specification. A reference anticipates compounds drawn to group I invention does not render obvious the compounds of other groups of invention. Contrary to applicant's assertion that groups I thru IX have the same classification, only group I compound is classified in class 546, subclass 156, group II compound is classified in class 549, subclass various dependent on the species elected, the classification of the inhibitor compound and the analog compound is undetermined since the structure is not defined, the search is therefore not co-extensive and is burdensome.

The search required for group I invention is not required for the other groups, the restriction requirement as indicated is therefore proper.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 14-16, 19-40, 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 1, what is 'a tail group'? According to the definition on page 17, 'tail group' 'includes groups that allow the compound of the invention to perform its intended function'. Which function? What are the structural requirement for these intended functions? A definition is not found in the specification. In another embodiment, the 'tail group' is 'hydrophobic'. However, the term "hydrophobicity" is a relative term which is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

b. For the compound Claims 19, 20, the term 'comprising' is open-ended and is therefore indefinite.

c. Claims 20-28, it is unclear whether these are compound claims, composition claims or method of use claims. Amending these claims in accordance to the proper format is recommended.

d. Claims 29, 32, the meaning of the term 'modulates' is unclear since it includes both enhancement and inhibition.

The rejection is applicable to claims dependent on the above claims.

Duplicate Claims

4. Applicant is advised that should claim 1 or 2 or 19 be found allowable, claims 20-27 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof since the use recited in claims 20-27 does not further limit the compound of claim 1, 2 or 19. Should claim 1 or 2 be

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found allowable, claims 29-30, 32 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof since the use recited in claims 29-30, 32 does not further limit the compound of claim 1 or 2. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

5. Claim 33 is objected to under 37 CFR 1.75 as being a duplicate of claim 34. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 1, 2, 4, 10-14, 19-28, 32-42, 46-48 are rejected under 35 U.S.C. 102(a) as being anticipated by Pesci (PNAS, 1999, 96(20):11229). Compound C, 2-heptyl-3-hydroxy-4-quinolone (Fig. 1), its composition, and method of use are encompassed by the instant claims.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 14, 15, 20-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Dekker (5942619 or WO 97/12868). Dekker's compound (columns 15-16, claim 1, fifth to

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eighth compound), and the composition thereof, are encompassed by the instant claims.

Although the biological activities of the compound as recited in the instant claims have not been described in the prior art, they are however, intrinsic to the compound. The compound isolated from the culture media in which *Pseudomonas aeruginosa* is grown as recited in claim 28 is identical to the prior art compound prepared by a different method.

10. Claims 1-4, 9, 12, 14, 20-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Guilhon (Phytochemistry, 1994, 37(4), 1193-1195).

The compound 3c (page 1193), the extract of the trunk bark, and the methanolic solution containing the compound, are encompassed by the instant claims 1-4, 9, 12, 14, 20-40.

The compounds 3a, 3b (page 1193), the extract of the trunk bark, and the methanolic solution containing the compounds, are encompassed by the instant claims 1, 14, 20-40. Although the biological activities of the compound as recited in the instant claims have not been described in the prior art, they are however, intrinsic to the compounds. The compound isolated from the culture media in which *Pseudomonas aeruginosa* is grown as recited in claim 28 is identical to the prior art compound prepared by a different method.

11. Claims 1, 14, 15, 20-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee (J. Liq. Chrom. & Rel. Technol., 1997, 20(1), 63-78).

The compounds 11, 16 (page 65), and the methanol-water crude extract containing the compound, are encompassed by the instant claims 1, 14, 20-40.

The compounds 12-15 (page 65), and the methanol-water extract containing the compounds, are encompassed by the instant claims 1, 14, 15, 20-40. Although the biological activities of the compound as recited in the instant claims have not been described in the prior art, they are however, intrinsic to the compounds. The compound isolated from the culture media in which *Pseudomonas aeruginosa* is grown as recited in claim 28 is identical to the prior art compound prepared by a different method.

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12. Claims 1-4, 12, 14, 20-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Beifuss (Synlett, 1997, 3, 313-315) .

The compound 8d (page 314, Table 3, entry 5) is encompassed by the instant claims 1-4, 12, 14, 20-34.

The compounds 8c, 8d (page 314, Table 3, entry 3, 4) are encompassed by the instant claims 1, 14, 20-34.

Although the biological activities of the compound as recited in the instant claims have not been described in the prior art, they are however, intrinsic to the compounds. The compound isolated from the culture media in which *Pseudomonas aeruginosa* is grown as recited in claim 28 is identical to the prior art compound prepared by a different method.

13. Claims 1-4, 12, 14, 20-40, 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Dibitus (J. Marine Biotechnology, 1998, 6, 136-141) .

The compound, 2-n-heptylquinol-4-one (page 139, Fig. 1), the extract and the culture medium containing the compound are encompassed by the instant claims 1-4, 12, 14, 20-40, 46.

The compound, 2-n-nonylquinol-4-one (page 139, Fig. 1) the extract and the culture medium containing the compound are encompassed by the instant claims 1, 14, 20-40, 46.

The compound, 2-n-nonylquinol-4-one (page 139, Fig. 1) the extract and the culture medium containing the compound are encompassed by the instant claims 1, 14, 15, 20-40, 46.

Although the biological activities of the compound as recited in the instant claims have not been described in the prior art, they are however, intrinsic to the compounds. The compound isolated from the culture media in which *Pseudomonas aeruginosa* is grown as recited in claim 28 is identical to the prior art compound prepared by a different method.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-42, 46-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification is only enabling for making and using 2-heptyl-3-hydroxy-4-quinolinone. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

a. *Nature of the invention.*

The instant invention is drawn to a compound of formula I as an autoinducer, useful for inhibiting the infectivity of *Pseudomonas aeruginosa*, thereby useful for treating an immuno-compromised subject infected thereof and is useful for regulating gene expression.

b. *State of the prior art and the level of the skill in the art.*

Autoinducer compounds for *Pseudomonas aeruginosa* have been shown to regulate gene expression and for treating infection of *Pseudomonas aeruginosa*. The homoserine lactone autoinducer has been described by Pearson (5591872), Bycroft (5593827) and Livinghouse (6337347). The quinolone autoinducer for *Pseudomonas aeruginosa* has been described by Pesci (see paragraph 7 above). Similar quinolone compound prepared by different methods are known (see paragraphs 9-13)

The level of the skill in the autoinducer art is high.

c. *Predictability/unpredictability.*

The high degree of unpredictability is well-recognized in the autoinducer art. A small change in the structure of the compound would drastically change its biological activity, as shown by the structurally similar autoinducer compounds (Bycroft, columns 18, Example 10).

While 2-heptyl-3-hydroxy-4-quinolone leads to the induction of las B'-lacZ, two structurally similar analogs are inactive as described on page 24 of the specification.

d. *Amount of guidance/working examples.*

• *How to make.*

Isolation, purification and identification of 2-heptyl-3-hydroxy-4-quinolone (PQS) from cultures of PAO-R1 (pages 28-29, Examples 2-4). This compound has also been synthesized (page 29, Example 5).

Starting materials and procedures for making the compound of formula I other than 2-heptyl-3-hydroxy-4-quinolone (especially those compounds wherein R10-R24 are other than hydrogen, and wherein R2-4 are all halogen, and the compounds wherein the 'tail' is not fully

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described) are not seen in the specification but are required. Sources are particularly pertinent especially when the structures of these compounds are not described. Absent sources, the public is offered mere language, rather than enablement. Ex parte Moersch 104 USPQ 122. In re Howarthe 210 USPQ 689.

- *How to use.*

The bioassay for the PQS is described on page 28 (Example 1). The result is shown in Fig. 6 (page 24). The inactivity in the bioassay of 2 PQS analogs is also described on page 24.

An example for a compound that ‘modulates’ the activity of PQS, either enhances or inhibits the antioinducer activity of PQS, ‘modulates’ or antagonize the activity of Las R and/or the RhIR proteins as recited in the instant claims 29-34 has not been described in the specification.

- e. *The breadth of the claims.*

Applicant’s assertion that all the structurally diverse compounds encompassed by the generic claims (including those compounds wherein R10-R24 are other than hydrogen, and wherein R2-4 are all halogen and the compounds wherein the ‘tail’ is not fully described), would be effective in inhibition of *Pseudomonas aeruginosa*, thereby useful for treating an immuno- compromised subject infected thereof and is useful for regulating gene expression in any bacteria does not commensurate with the scope of the objective enablement, especially in view of the high degree of unpredictability in the art, and the working examples limited only to 2-heptyl-3-hydroxy-4-quinolone (paragraphs c-d above).

- f. *Amount of undue experimentation.*

Since insufficient teaching and guidance are provided in the specification (paragraph c-e above), one of ordinary skill in the art, even with high level of skill, would not be able to make and use all the invention as claimed without undue experimentation except for making and using 2-heptyl-3-hydroxy-4-quinolone.

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Specification/ Drawings

15. The specification is objected to because the figures in the specification do not come within the purview of 37 CFR 1.58(a), which permits only tables, chemical and mathematical formulas in the specification in lieu of formal drawings.

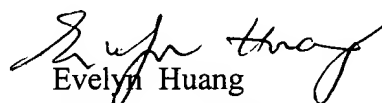
Formal drawings in accordance to 37 C.F.R. 1.81, 1.83-1.85 are required. See MPEP 608.01 and 608.02.

A brief description of the drawings is not found in the specification but is required.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 703-305-7247. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 703-308-4698. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


Evelyn Huang
Primary Examiner
Art Unit 1625

August 23, 2002